comparable to those in previous reports. In the present investigation, due to the retrospective nature of the study design, the level of anastomosis was calculated from the tumor location and distal resection margin when data were not available. And in some patients, tumor location was measured only by digital examination and not by rectoscopy, these might introduce bias. Although the anastomotic level was not associated with leakage, this data should be evaluated with caution.

High ligation of IMA was the only leakage risk factor on univariate analysis in the present study. Lange et al. [24] systematically reviewed the literature concerning the level of ligation and concluded that preserving IMA and left colic artery was anatomically less invasive with respect to circulation and autonomous innervations of the proximal limb of anastomosis. Seike et al. [25] measured the colonic blood flow at the proximal site of the anastomosis by laser Doppler flowmetry to evaluate the influence of high ligation. They proved a significant reduction of colonic blood flow at the proximal site after clamping IMA. Our result also suggested the possibility that blood flow reduction on anastomotic sites leads to more leakage.

In the present study, we reported our low leakage rate in cases without DS (11.5%; 24 of 209). This rate is comparable to the leakage rate in cases with DS in a randomized controlled trial by Matthiessen et al. (10.3%; 12 of 116) [1]. This may have some association with our patient population that neoadjuvant radiotherapy or chemo-radiotherapy was not performed in this series. Neoadjuvant radiation therapy is considered to be a risk factor by some authors [13, 14]. Although randomized multicenter trials have shown that neoadjuvant radiation does not increase postoperative morbidity [26–28], Peeters et al. [18] retrospectively analyzed risk factors from the database of the Dutch Colorectal Cancer Group, and reported that a defunctioning stoma was constructed more often in patients who had received radiation, and that the absence of a DS was significantly associated with a higher leakage rate.

We also reported our low mortality. This reflects our low leakage rate in cases without DS and our appropriate decision of reoperation for peritonitis in cases without DS. We considered that our appropriate decision lead to low mortality rate and high reoperation rate (54.2%). In the present study, a DS constructed at the time of initial surgery obviously reduced the necessity of an urgent reoperation after overt leakage, proving the clinical benefits of DS in this regard. The important objective of DS was not to eliminate leakage but to decrease the risk of reoperation. However, DS construction did not guarantee the complete safety of LAR. In fact, we experienced one mortality in a patient with DS in this series, so complete elimination of leakage and severe septic complications was not feasible.

In conclusion, we clearly demonstrated the outstanding safety of LAR with very low mortality and acceptable leakage rate in our group. Although this retrospective study could not prove whether DS can prevent leakage itself, we found that it could mitigate the need for urgent abdominal reoperation for leakage. To define clear criteria for DS construction, a well-designed randomized control study is genuinely needed in the future.

Acknowledgments This study was supported by the "Studies on the standardization for diagnosis, treatment, and follow-up of colorectal cancer patients", sponsored by Grant-in-Aid 18-2 for Cancer Research from the Ministry of Health, Welfare and Labor of Japan. The authors thank the following surgeons for generously providing data: S. Yamamoto (National Cancer Center Hospital), S. Noura (Osaka Medical Center for Cancer and Cardiovascular Diseases), Y. Komori (Aichi Cancer Center Hospital), and T. Kobatake (National Hospital Organization Shikoku Cancer Center Hospital).

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Journal of Surgical Oncology 2010;102:778–783

Preliminary Experience With Bladder Preservation for Lower Rectal Cancers Involving the Lower Urinary Tract

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Background and Objectives: The aim of this study was to evaluate the feasibility of en bloc colorectal resection combined with radical prostatectomy as an alternative to total pelvic exenteration (TPE) for patients with locally advanced rectal cancer involving the lower urinary tract organs.

Methods: Twenty men with primary rectal cancer clinically involving the lower urinary tract organs underwent extended colorectal resection combined with radical prostatectomy. Data were entered prospectively into a database. Oncological and functional outcomes were analyzed.

Results: Anal sphincter-preserving operation (SPO) with radical prostatectomy was performed in 12 patients, abdominoperineal resection with radical prostatectomy in 8, and urinary reconstruction in 16. Morbidity and mortality rates were 35.0% and 0%, respectively. Five-year overall and disease-free survival rates were 83.6% and 42%, respectively. The cumulative 5-year local recurrence rate was 20.0%. All patients with urinary reconstruction achieved good voiding function, and patients with SPO showed acceptable anal function.

Conclusions: For lower rectal cancers involving lower urinary tract, en bloc rectal resection combined with radical prostatectomy appears oncologically acceptable and can reduce the number of TPEs.

J. Surg. Oncol. 2010;102:778–783. © 2010 Wiley-Liss, Inc.

KEY WORDS: **total pelvic exenteration; abdominoperineal resection; intersphincteric resection; radical prostatectomy; cysto-urethral anastomosis**

INTRODUCTION

The standard surgery for locally advanced rectal cancer located within 5 cm from the anal verge is abdominoperineal resection (APR) [1]. With tumor involvement of the base or trigone of the bladder and of the prostate, total pelvic exenteration (TPE) may be required to achieve negative margins [2]. These patients often require double stomas, one for urinary diversion such as an ileal conduit, and another for fecal diversion such as a sigmoid colostomy. This procedure may thus compromise quality of life.

Recent advances in sphincter-preserving operations (SPO) including intersphincteric resection (ISR) and ultra-low anterior resection (U-LAR) for very low rectal cancer have allowed colo-anal anastomosis (CAA) or colo-anal canal anastomosis to be performed without adverse effects on outcome [3–7]. Furthermore, neobladder construction has also become a standard surgery following cystoprostatectomy for invasive bladder cancer [8,9]. Conversely, en bloc radical prostatectomy seems to represent an option in selected patients who would otherwise need TPE for locally advanced rectal cancer involving the prostate [10–13]. In this procedure, the bladder is preserved to allow voiding via the urethra with urinary continence. Together, these advances may improve postoperative quality of life for patients with locally advanced rectal cancer requiring TPE, enabling surgery to be performed without a stoma or with only a single stoma [14–17]. These approaches have been explored as alternatives to TPE in 20 patients with locally advanced primary rectal cancer at our institute since 2001.

In this prospective study, radical prostatectomy for locally advanced primary rectal cancer was evaluated clinically. The current series differs from the original in the number of patients excluding recurrent cases, longer follow-up, and use of a scoring system for anal function [17]. Informed consent was obtained from all patients, and institutional review board approval for this study was also obtained. This study has been performed in accordance with the Helsinki Declaration of 1975 and 1983.

METHODS

Patients

Between January 2001 and December 2008, a total of 20 patients with locally advanced primary rectal cancer clinically involving the prostate underwent extended colorectal resection combined with radical prostatectomy at the National Cancer Center Hospital East. All 20 patients were originally considered candidates for TPE. However, the urinary bladder was preserved in 20 patients as an alternative to TPE. Although preoperative radiochemotherapy for resectable rectal cancer is not a standard protocol in Japan, four

Abbreviations: APR, abdominoperineal resection; TPE, total pelvic exenteration; SPO, sphincter-preserving operation; ISR, intersphincteric resection; U-LAR, ultra-low anterior resection; CUA, cysto-urethral anastomosis; CAA, colo-anal anastomosis.

Grant sponsor: Ministry of Health, Labor, and Welfare of Japan; Grant number: 030.

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Received 26 March 2010; Accepted 26 July 2010

DOI 10.1002/jso.21717

Published online 1 September 2010 in Wiley Online Library (wileyonlinelibrary.com).

TABLE I. Patients and Clinical Characteristics, 2001–2008 (n = 20)

Mean age, years (range)	64 (43–76)
Mean distance from AV, cm (range)	3.0 ± 1.1 (0–4.2)
Depth of invasion (clinical)	cT3, 2[a]; cT4, 18
Involving organs	P, n = 11; P + SV, n = 3; P + SU, n = 4; combined with prostatic cancer, n = 2[a]
Node involvement (clinical)	cN (−), n = 5; cN (+), n = 15

AV, anal verge; P, prostate; SV, seminal vesicle; SU, sphincter urethrae muscle.
[a]Rectal cancer with synchronous primary prostatic cancer.

patients agreed to undergo preoperative radiochemotherapy according to our previous protocol [6]. During the same period of time, we performed only five TPEs for locally advanced primary rectal cancer involving a wide-ranging area of the urinary bladder and prostate in male patients.

Rectal tumor was staged according to the 6th UICC TNM staging system. Age, level of tumor, and clinical tumor stage for the 20 patients are given in Table I. Although two of these patients displayed cT3 tumors with synchronous primary prostatic cancer, adequate margins were not clinically evident between the rectal tumor and the prostate. Therefore, these two patients were included in this study. Mean patient age was 64 years (range: 43–76 years), and mean distance from tumor to anal verge was 3.0 cm (range: 0–4.2 cm). To determine the distance of the rectal tumor to the anal verge, rigid proctoscopy with measurement, and/or digital examination were used.

Preoperative staging was conducted using transanal digital examination, computed tomography (CT), magnetic resonance imaging (MRI), endoscopic ultrasonography, colonoscopy, and barium enema. Position emission tomography was also performed preoperatively to exclude multiple metastatic disease. All patients in this study showed localized rectal tumor involving the prostate and seminal vesicle, or combined with carcinoma of the prostate, without distant metastases evident preoperatively. Clinicopathological findings were examined in all resected specimens. Involvement of adjacent organs and surgical margins, perioperative morbidity and mortality, locoregional control, overall survival (OS), and disease-free survival (DFS) were investigated. Urinary and anal functions were also evaluated postoperatively by monitoring continence and voiding habits. Fecal evacuation functions were investigated using both Wexner score [18] and Kirwan grade [19].

Indications and Surgical Procedure

Bladder-sparing extended en bloc rectal resection combined with radical prostatectomy was considered if the cancer was clinically fixed to the prostate or bladder, or if an adequate margin between the tumor and these organs seemed impossible to achieve as judged from MRI and CT. Patients undergoing this surgical procedure had a residual urinary bladder with available capacity ≥50 ml and with the possibility of cysto-urethra anastomosis (CUA). Distant metastasis, wide-ranging involvement of the urinary bladder and prostate, or marked pelvic lymph node metastasis were generally considered contraindications for this operation, as preservation of the available urinary bladder was impossible in patients with wide-ranging involvement of the urinary bladder. If the patient showed wide-ranging involvement of the urinary bladder and prostate, TPE was performed.

Surgical technique was as follows. The patient was placed in the lithotomy position. Total mesorectal excision with lateral pelvic node dissection was performed, although lateral node dissection is not standard care outside of Japan. Ureters were visualized and carefully protected throughout the procedure, and the superior vesical artery was preserved bi- or unilaterally. At this time, the status of involvement between the rectum and the base of the bladder was investigated. After confirming the absence of wide-ranging involvement of the urinary bladder, bladder-sparing surgery was deemed possible. The rectal cancer, prostate and seminal vesicles were resected en bloc as a cooperative venture between colorectal and urological surgeons using the usual methods for radical prostatectomy and ISR or APR. APR was performed when safe surgical margins could not be obtained by ISR. Confirmation of cancer-free radial and distal margins was then performed in the resected specimen using frozen sections to evaluate the extent of pelvic invasion, and to determine whether limited resection was possible. If tumor invasion was suspected in surgical margins from intraoperative histological examination, the operative procedure was converted to TPE. After confirming preservation of the membranous urethra and bladder, the bladder neck was reconstructed and a CUA was created by urological surgeons. When the sphincter urethrae muscle was sacrificed due to probable tumor invasion, a cystostomy was created for voiding through a catheter. Finally, a CAA with diverting stoma or permanent colostomy was established by colorectal surgeons.

The bladder catheter was left for 2 or 3 weeks and removed after cystography revealed an intact anastomosis. The diverting stoma was closed 3 months after radical surgery.

Adjuvant Therapy

Four patients (clinical T4, N2: n = 3; clinical T4, N1: n = 1) agreed to undergo preoperative radiochemotherapy according to our old-fashioned protocol between 2001 and 2002, although preoperative radiochemotherapy for resectable rectal cancer, even in those patients undergoing TPE, is not standard in Japan. These patients received 45 Gy in the whole pelvis over a 5-week period, followed by resection after ≥2 weeks. In addition, 5-fluorouracil (5-Fu) was administered as a continuous infusion at 250 mg/m^2/day during radiotherapy to enhance radiotherapeutic efficacy. Postoperative chemotherapy (5-Fu/leucovorin therapy) was offered to patients with pathological stage III.

Follow-Up

Mean duration of follow-up was 40 months (range: 4–106 months). Follow-up examinations were performed every 3 or 4 months for 2 years postoperatively, then every 6 months thereafter. Patients underwent clinical examination, laboratory tests including tumor marker levels, and lung, liver, and pelvic CT. Investigation of functional status for voiding and evacuation was also performed using our questionnaire on the status of voiding and bowel functions based on continence, frequency, soiling, urgency, and discrimination. These functions were evaluated at 3, 6, 12, and 24 months postoperatively using Wexner score [18] and Kirwan classification [19]. Physiological assessment was also performed using anal manometry and uroflowmetry.

Statistical Analysis

The starting point for survival and recurrence-free intervals was the day of operation, and data on patients who were alive or free of recurrence were censored at the last follow-up. OS was defined as the time from radical surgery until death from any cause. Local recurrence was defined as recurrence confined to the pelvis and distant recurrence as recurrence present outside of the pelvis. Statistical evaluations were undertaken using the SPSS for Windows version 11.0J software (SPSS-Japan, Tokyo, Japan). OS and DFS curves were calculated using the Kaplan–Meier method.

RESULTS

Operation Type

Eighteen patients showed localized tumors clinically involving the prostate, two had clinical T3 lower rectal tumors with synchronous primary prostatic cancer. No procedures were converted to TPE because of inadequate margins during the period of this study. Twelve patients underwent anal SPOs (ISR, n = 11; U-LAR, n = 1) with radical prostatectomy, and 8 patients received APR with radical prostatectomy because the lower edge of the tumor was very close to the anal verge or the tumors clinically involved the external anal sphincter. Urinary reconstruction was performed in 16 patients using CUA, while cystostomy was established in four patients because of intraoperative histological probability of cancerous invasion to the sphincter urethrae muscle. As a result, 12 patients were without stoma, four patients had a single stoma, and a fecal stoma and cystostomy were used in four patients (Table II).

Median operative time was 495 min (range: 416–628 min), and median intraoperative blood loss was 2,200 ml (range: 1470–6172 ml). Median duration of hospitalization was 25 days (range: 21–38 days).

Pathological Findings

All resected margins were examined pathologically and confirmed as cancer-free. Final pathological examination revealed pT4 in eight patients (40.0%). Histological cancerous invasion of the prostate was revealed in seven patients. Nine patients showed pT3 tumor with fibrosis or inflammatory changes surrounding the tumor, and three patients displayed pT2 tumor with the same histological changes. Two of three patients with pT2 tumor had synchronous primary prostatic cancer (pT1c). It seemed to be difficult to separate the rectal tumors safely from the prostate during operation in these patients with pT3 or pT2 tumors. Curative resection was achieved in all 20 patients by bladder-preserving surgery.

Morbidity and Mortality

Morbidity for this series is shown in Table III. No postoperative complications were seen in 13 patients. Of the seven patients (35.0%) who suffered from some form of complication, cysto-urethral anastomotic leak was identified in five patients, requiring catheterization through the anastomosis site for 3–24 weeks postoperatively. However, none of these cases developed urethral stricture. Incidence of cysto-urethral anastomotic leak was significantly higher in patients with APR (75.0%, 3 of 4) than in patients with SPO (16.7%, 2 of 12; $P < 0.05$). In particular, anastomotic urethral leak was a major complication in patients undergoing APR with CUA (Fig. 1), requiring special care during the long postoperative course. Colo-anal anastomotic leak was only observed in 1 of the 12 patients with SPO. This patient suffered from colo-anal anastomotic stenosis before closure of the diverting ileostomy. Additional plastic surgery for anastomotic stricture was thus performed by plastic surgeons. After that, the diverting stoma was closed at 14 months after initial operation. Other complications included pelvic abscess (20.0%, 4 of 20), wound infection (15.0%, 3 of 20), and bowel obstruction (5.0%, 1 of 20). No postoperative mortality was encountered in hospital or within 30 days postoperatively.

TABLE II. Operation Type and Pathological Findings

Surgery types	ISR with RP, n = 11; APR with RP, n = 8; V-LAR with RP, n = 1
Reconstruction	Urinary...CUA, n = 16; CS, n = 4 Fecal...CAA, n = 11; CACA, n = 1; stoma, n = 8
Depth of invasion (pT)	pT4, n = 8 (40.0%); pT3, n = 9; pT2, n = 3
Involving organs	P, n = 7; ES, n = 2; SV, n = 1 (prostatic cancer, n = 2)
Node involvement (pN)	pN0, n = 11; pN1, n = 4; pN2, n = 3
Surgical margins	Negative, n = 20; positive, n = 0

No stomas, n = 12; single stoma, n = 4; CS + stoma, n = 4.
ISR, intersphincteric resection; APR, abdominoperineal resection; PR, radical prostatectomy; SPO, sphincter-preserving operation; CUA, cysto-urethral anastomosis; CS, cystostomy; CAA, colo-anal anastomosis; CACA, colo-anal canal anastomosis; ES, external anal sphincter.

TABLE III. Postoperative Complications (n = 20)

Anastomotic leakage	5/16 (31.3%) CUA: 5/16 SPO with CUA: 2/12 (16.7%)* APR with CUA: 3/4 (75.0%)* CAA, CACA: 1/12
Pelvic abscess	4/20 (20.0%)
Wound infection	3/20 (15.0%)
Ileus (small bowel)	1/20 (5.0%)
Overall morbidity	7/20 (35.0%)
Mortality	0/20 (0%)

*$P < 0.05$.

Survival

As of the last follow-up in December 2009, 15 patients were alive and 5 were dead. Causes of death included multiple bone metastases (n = 2), multiple lung metastases (n = 1), multiple liver metastases (n = 1), and multiple liver and lung metastases (n = 1). Estimated 5-year overall and DFS rates were 83.6% and 42.0%, respectively (Fig. 2).

Local and Overall Recurrence

A total of 10 patients (50.0%) developed recurrence (Table IV). Incidence of recurrence was 10.0% for local recurrence, 35.0% for lung metastases, 15.0% for liver metastases, and 10.0% for bone metastases. These local recurrences developed in the presacral area, and in the perianastomotic site of the CUA. Patients with local recurrence successfully underwent tumor resection with sufficient surgical margins. Intraoperative radiotherapy was therefore not administered. One of these patients was alive with no evidence of disease after resection of local recurrence, and 2 of 3 patients with liver metastasis were also alive and disease-free after hepatic resection. Cumulative 5-year local recurrence rate was 20.0% in this series.

Postoperative Urinary and Anal Functions

Urinary function was evaluated in 16 patients with CUA and anal functions were also investigated in 11 patients with SPO who were followed for ≥12 months after stoma closure (Table V). All 16 patients with CUA were able to void via the urethra, with little or no residual urine (range: 0–70 ml) and without the need for intermittent self-catheterization. All patients also showed complete daytime urinary continence. Median voiding volume at one time was 245 ml (range: 150–350 ml). Overflow incontinence at night was occasionally experienced over the course of 2 years postoperatively.

The four patients who underwent catheter-cystostomy passed urine via an inserted catheter. Voiding style was similar to that of patients with an ileal conduit. Unfortunately, erectile function could not be preserved in any of the 20 patients.

Of the 12 patients who underwent SPO with radical prostatectomy, 11 received closure of a diverting stoma and 1 died of multiple liver metastases before stoma closure. Anal functions were evaluated in

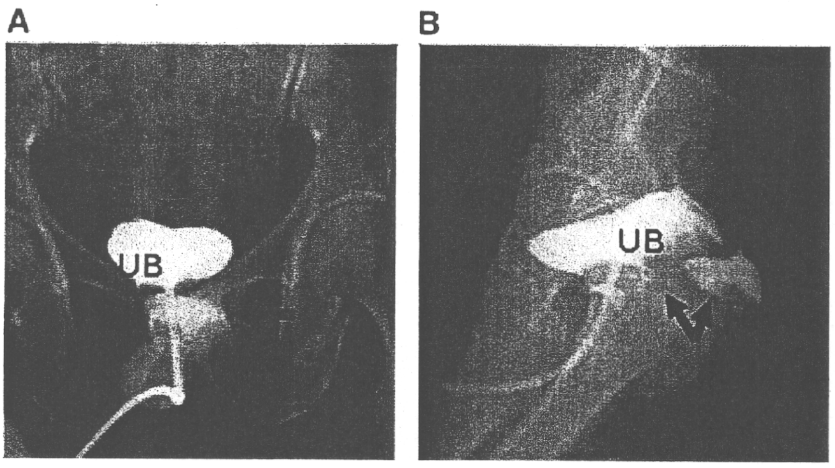

Fig. 1. Cysto-uretheral anastomotic leak in a patient undergoing APR with CUA. A: Front of view in postoperative retrograde cystogram. B: Lateral of view in postoperative retrograde cystogram. Arrow indicates collection of leakage. UB, urinary bladder.

these 11 patients. Wexner scores and Kirwan classification for the 11 patients are shown in Table V. None experienced complete incontinence, although one patient suffered occasional major soiling (Kirwan grade 4) for about 1 year after closure of the diverting stoma. Five of the 11 patients experienced minor soiling, particularly at night. These patients passed fewer than 6 bowel movements per day, 2 patients had incontinence of flatus, and 8 patients wore pads. Median Wexner score in the 11 patients was 11.5 (range: 0–15). Anal functions tended to improve gradually during the second year after stoma closure.

DISCUSSION

Orthotropic neobladder surgery is often attempted as an alternative for patients undergoing radical cystectoprostatectomy for bladder cancer, to enable voiding via the urethra with urinary continence [14,15]. Patients undergoing radical prostatectomy with CUA for carcinoma of the prostate can also void with continence via the urethra. On the other hand, SPOs for lower rectal cancer have been becoming more common with the introduction of improved surgical techniques such as ISR, which was devised in the 1980s, and these modern concepts were established in the 1990s. ISR is now defined as a procedure obtaining sufficient surgical margins by removing part or all of the internal anal sphincter and restoring bowel continuity for patients with rectal cancer located within 5 cm from the anal verge. Fixation to the lower urinary tract organs in primary locally advanced rectal cancer is not uncommon in male patients. Standard therapy for such patients with the absence of extra-pelvic metastases has traditionally been pelvic exenteration, to ensure negative surgical margins. However, this procedure sometimes requires urinary and fecal diversion. Double stomas are therefore sometimes needed.

In 1966, separate prostatectomy was suggested as a routine additional procedure to prevent voiding problems after APR for rectal cancer. More recently, three patients with synchronous rectal and prostate cancer who underwent separate dissections were reported [10]. Other reports have described combined radical retropubic prostatectomy and proctosigmoidectomy en bloc in 11 selected patients with the cancer fixed only to the prostate [11–13,16].

We believe that even more limited excision is feasible and preferable if the tumor can be removed en bloc. We also think some of these patients may be allowed preservation of the prostate if they had significant tumor shrinkage by neoadjuvant therapy such as preoperative chemoradiation or chemotherapy. However, preoperative radiochemotherapy for advanced rectal cancer, even in those patients undergoing TPE, is not a standard option in Japan. Moreover, preoperative radiotherapy or radiochemotherapy may affect postoperative complications and various functions. Since 2001, we have used a combined approach in 20 patients with primary rectal cancer involving lower urinary tract organs or combined with synchronous prostatic cancer. In our series, the bladder was preserved in all patients, and anal SPOs using ISR techniques were performed wherever possible, obtaining cancer-free margins in all patients. These procedures without ISR were first reported by Campbell et al. [11]. In their report of two patients, en bloc excision yielded negative surgical margins with no evidence of local recurrence at 1-year follow-up

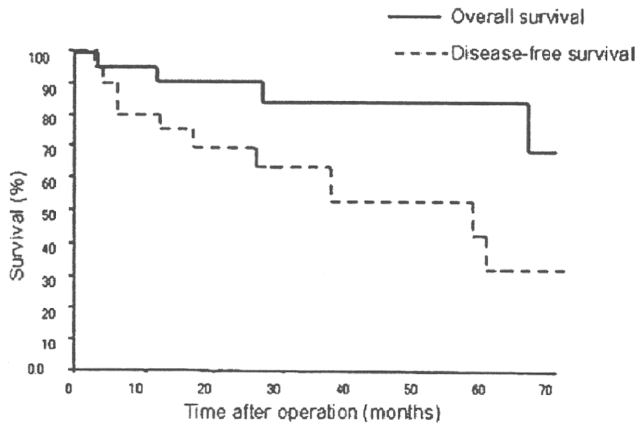

Fig. 2. Overall and disease-free survival rates among 20 patients who underwent bladder-preserving surgery.

TABLE IV. Patients With Recurrence (n = 20)

Recurrences	Number of patients (n = 10)	Salvage operation
Lung	7 (35.0%)	
Liver	3 (15.0%)	Resection, n = 3 → ANED; 2
Bone	2 (10.0%)	
Loco-regional	2 (10.0%)	Resection, n = 2 → ANED; 1
Distant lymph node	1 (5.0%)	AWD; 1
Median follow-up, months (range): 40 (4–106)		

ANED, alive with no evidence of disease; AWD, alive with disease.

TABLE V. Postoperative Functions (12 Months After Operation)

Reconstruction	Voiding	VV (ml), median (range)	RV (ml), median (range)
Urinary function			
CUA, n = 16	Spontaneous continence	245 (150–350)	5 (0–70)
CS, n = 4	Incontinence	Catheterization	
Anal function (SPO, n = 11)			
Kirwan grade[a]	I, n = 3; II, n = 2; III, n = 5; IV, n = 1; V, n = 0		
Wexner score	11.5 (0–15), median (range)		

VV, voided volume; RV, residual volume; Grade I, perfect; Grade II, incontinence of flatus; Grade III, occasional minor soiling; Grade IV, frequent major soiling; Grade V, incontinent (requiring colostomy).
[a]Kirwan classification.

examination, and patients displayed satisfactory control of bowel and voiding function. In a report by Wiig et al. [16], six patients underwent en bloc radical prostatectomy for locally advanced or recurrent rectal cancer involving the prostate. During 10–50 months of follow-up, none of these patients developed local recurrence, 4 of the 5 patients with CUA showed good quality of life and none wanted an ileal conduit.

In our previous report with a median follow-up period of 26 months, no sign of local recurrence was seen in 11 patients who underwent the same operation for locally advanced or recurrent rectal cancer involving the prostate and seminal vesicles [17]. Few patients with long-term follow-up were examined in these previous reports [11,16,17]. Deciding whether these procedures represent a reasonable operation was thus difficult, due to a lack of published reports with long-term follow-up.

However, the present study showed that two patients (10.0%) developed local recurrence during follow-up. In one of these patients, recurrence occurred in the presacral area. Local recurrence does not seem likely to have been prevented if the patient had undergone TPE. This patient underwent successful resection of the recurrent tumor. However, this patient died of multiple lung metastases at 85 months after initial operation. Another local recurrence developed at the perianastomotic site of CUA. This patient also received resection of the recurrent tumor and underwent cystostomy. The patient remains alive and disease-free at follow-up (106 months). An acceptable 5-year OS (83.6%) was obtained in patients undergoing the same operation for primary locally advanced very low-lying rectal cancer during a mean follow-up of 40 months (range: 4–106 months), although 5-year DFS was not so good. Despite our concerns about the risk of local recurrence after limited excision to preserve the urinary bladder, local recurrence rate in this series was relatively low. We think that a remaining problem is the prevention of distant metastases. To date, these procedures appear oncologically safe in selected patients with rectal cancer involving the prostate.

Moreover, patients with CUA reported satisfactory control of voiding function. Voiding style resembled that of patients with an ileal neobladder. Unfortunately, four patients required cystostomy because the sphincter urethrae muscle was sacrificed due to the probability of cancerous invasion. These patients voided via an inserted catheter that was exchanged once a month, much like patients with an ileal conduit. An obvious difference between neobladder and bladder-sparing surgery is that the neobladder is made using intestine, which results in inevitable long-term complications such as mucus production, nutritional abnormalities, metabolic acidosis, skeletal demineralization, and the risk of malignant transformation in the intestinal segment [20,21]. No such problems are associated with bladder-sparing surgery.

Patients with SPO using ISR also reported satisfactory control of anal function, even though they experienced occasional minor soiling, urgency, fragmentation, and frequent bowed movements. In patients undergoing ISR for lower rectal cancers, almost all patients were able to achieve acceptable anal function according to our and other reports [4,6,7,22–24]. Status was Grade I, II, or III in the Kirwan classification, and few patients showed incontinence (Kirwan Grade V). In the present series, acceptable anal function was achieved using these procedures, and permanent colostomy was not required.

Conversely, the complication rate was relatively high in terms of leakage from CUA. In the present series, anastomotic urethral leak was observed in 5 (31.3%) of 16 patients with CUA. Wiig et al. [16] also reported that 3 of 6 patients with CUA had anastomotic urethral leak with one major leakage. In particular, the frequency of anastomotic leaks was significantly high in patients undergoing APR with CUA. However, urethral anastomotic leak rate was less in patients undergoing ISR or ultra-LAR with CUA, as the neorectum was present behind the CUA. Some reports have examined the leakage rate from CUA in patients undergoing radical retropubic prostatectomy only [25,26], finding no evidence of extraversion in 135 (75%) of 179 cystograms, and a clinical prolonged leakage rate of 0.6% (11/1796). All of these patients had the rectum behind the CUA. Urethral anastomotic leaks are thus probably due to a lack of supporting tissue behind the anastomosis when the rectum has been removed in patients who have received APR. Measures to prevent urethral anastomotic leakage by introducing a flap of greater omentum behind the anastomosis or other additional flap operations such as gracilis flap thus appear warranted.

CONCLUSION

In this series, en bloc rectal resection combined with radical prostatectomy was successfully performed in 20 men, even though these patients had been considered as candidates for standard TPE. Acceptable curability and postoperative urinary and/or anal functions could be achieved with this procedure, although the complication rate was relatively high. More experience and longer follow-up evaluations are necessary to define the operative morbidity, risk of recurrence, and functional results associated with these procedures. However, if the bladder and anal sphincter are spared, the procedures described offer several advantage over TPE.

We conclude that en bloc rectal resection combined with radical prostatectomy may produce acceptable curability and good functional results in selected patients with lower rectal cancer involving the lower urinary tract organs. These procedures may become an option for selected patients who would otherwise need TPE for locally advanced rectal cancer involving the prostate.

ACKNOWLEDGMENTS

This study was supported in part by third-term Comprehensive Control Research for Cancer grant #030 from the Ministry of Health, Labor, and Welfare of Japan. We also wish to thank the staff in the Department of Pathology at our institute for the pathological investigations in this study.

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腹腔鏡下直腸癌手術における前壁剝離の工夫

Dissection tips in anterior rectal laparoscopy for rectal cancer

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キーワード　直腸癌　腹腔鏡下手術　前壁剝離　骨盤底

要旨： 腹腔鏡下直腸癌手術では手技を定形化することでスムーズな術野展開が得られ，手術を円滑に施行することができる．しかし，直腸前壁の剝離に関しては術野展開の困難な場面に遭遇することがよくある．本稿では，前壁剝離の基本的な手技および術野展開の難しい症例に対して工夫している点を呈示する．子宮の垂れ込みによって術野展開が困難な女性では子宮マニピュレーターを使用し，体外から子宮を展開する．また，術中に子宮に直針をかけて腹側に牽引することで視野が確保される．男性の場合は膀胱直腸窩近傍の腹膜に直針をかけて頭側・上方向に牽引することで鉗子による術野展開をサポートすることができる．

はじめに

腹腔鏡下手術の適応は拡大しており，全国アンケート調査の最新の報告でも結腸癌だけでなく，直腸癌治療においてもその症例数は増加傾向にある[1]．現在，直腸S状部までの癌はJCOG0404による長期成績の報告を待っている状況にあるが[2]，実診療では腹腔鏡下手術の標準化が進んでいる．一方，手術手技の難易度が高い上部直腸以下の症例に対しては研究プロジェクト（LAPRC）によってその安全性が検討されており[3]，腹腔鏡下直腸癌手術の標準化が目指されている．

腹腔鏡下前方切除術では剝離部位ごとの術者と助手の役割を明確にすることでスムーズな術野展開が得られる．当院ではすべての腹腔鏡下手術を経験の豊富な常勤医師1名とレジデント2名の組み合わせで行っており，個々の手術ごとに異なるチーム編成となっている．レジデントは経験年数や習熟度に応じてスコピストから術者までを経験する．術者と助手の役割を定形化することは，レジデントの手技習得を教育するうえで大きく寄与していると思われる．また，術野展開において助手の担う役割は大きく，助手から術者にステップアップする過程で助手の役割を自覚し，よりよい術野展開方法に精通することが重要である．

直腸周囲の剝離手技のなかでも，直腸前壁の剝離では子宮の垂れ込みや骨盤底の深さによって術野の展開に難渋する場面に遭遇することがよくある．本稿では，前壁の剝離に関して基本的な手技と，われわれが工夫している点について述べる．

手術手技

1．基本手技

恥骨上を含めた5ポートを基本としている．腹腔鏡下前方切除術の基本手技は，剝離部位ごとに図1に示した7つの場面に分けて手術を進めていく．

2．前壁剝離の基本（図2）

恥骨上のポートからの腸鉗子で腫瘍口側の直腸を大きく把持し，頭側に牽引して固定する．この際に把持した腸管や間膜を損傷しないように十分に注意する．

術者は剝離部位の直腸側を頭側に牽引しながら剝離を進めていくので，助手は剝離部位に合わせ

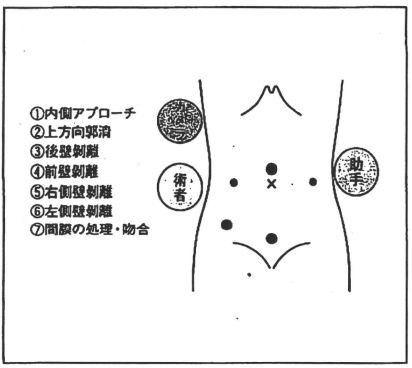


図1　腹腔鏡下前方切除の定形化
術者，助手，スコピストの3名で5ポートを基本とし，剝離部位によって7つの場面に分ける．

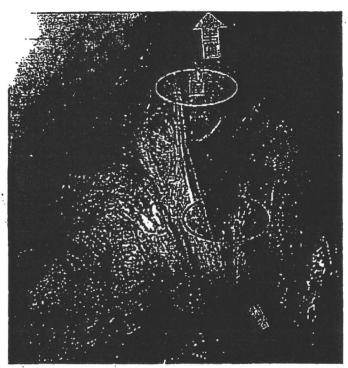


図2　前壁剝離の基本
前壁（腟や精嚢，前立腺）に腹側への緊張をかける．

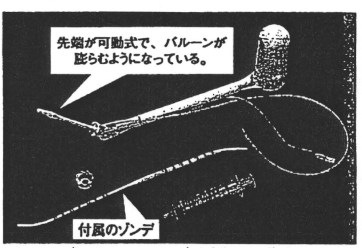


図3　エンドパス・ユーテリン・マニピュレーター

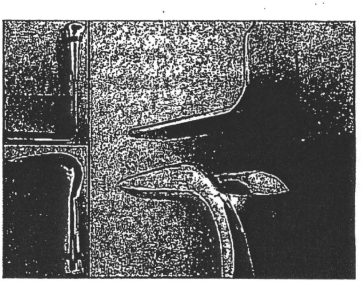
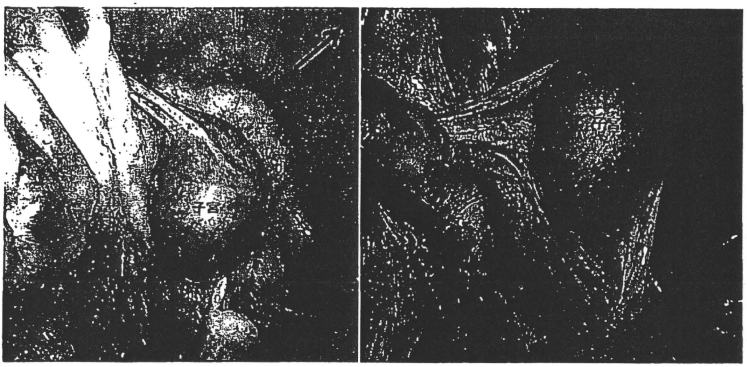


図4　ジモン式腟鉤
上葉と下葉に分かれている．

て前壁（腟後壁側や精嚢，前立腺にあたる部位）を上方向に牽引する．腟などは鉗子で把持すると損傷・出血することがあるので，鉗子の先端をハの字に開いて，腹側に押し上げることで視野作りが有効になる．



a b

図5　マニピュレーターの操作

a：挙上前．b：挙上後．体外からマニピュレーター本体を操作することで，さらに腹側方向の緊張をかけることができる．矢印は腹側方向．

（女性症例の場合）

（1）マニピュレーター

術前の CT などで子宮の大きいことが予測される症例については，執刀の前に子宮にマニピュレーターを挿入している．当院ではエンドパス・ユーテリン・マニピュレーター（ジョンソン・エンド・ジョンソン社）を使用している（図 3）．ジモン式腟鉤（図 4）で外子宮口を展開し，付属品のゾンデ・ダイレーターで子宮の奥行きと方向を確認してから本体の先端をゾンデに沿わせて挿入すると入れやすい．抵抗なく挿入できたら子宮内で先端のバルーンを膨らませることによって子宮内での位置を固定することができる．

クスコで外子宮口を展開するとマニピュレーターを挿入したあとにクスコが抜けなくなるので，上葉と下葉に分かれるジモン式腟鉤が有用である．挿入後は右大腿部内側にテープで固定している．

術中は気腹時から子宮が上方腹側に立ち上がるように保持されている．腟近傍の剝離の際には，体外からマニピュレーター本体を操作することで，さらに腹側方向の緊張をかけることや左右の緊張をかけることができる（図 5）．

本器具を抜去したあとに子宮から出血を認める場合があるが，ほとんどは自然に止血される．当院での経験はないが，出血が続く場合はタンポンを挿入することで止血することが可能である．

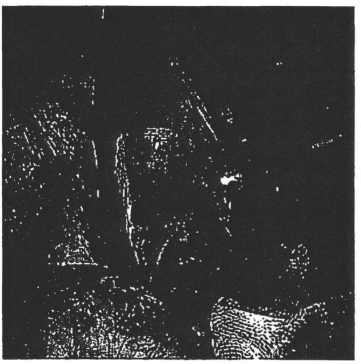


図6　子宮の吊り上げ

1 針でも有効な視野を得ることができる．

（2）子宮の吊り上げ（図 6）

執刀の前にマニピュレーターを挿入しなかった症例や，挿入していても子宮筋腫が大きく子宮の挙上が不十分な場合などは，恥骨上で体外から直

図7　男性症例の前壁
左右1か所ずつ腹膜にかけて腹側に吊り上げることで，骨盤低トンネルの天井を持ち上げることができる．

針付きの2-0ナイロン糸を刺入し，子宮体部にかけることで子宮を吊り上げている．恥骨上の左側から直針を刺入して子宮体部の右側にかけて子宮全体を左頭側に牽引することで1針でも有効な視野を得ることができる．1針のみでよい視野が確保されないときや，直腸前壁の剝離をさらに肛門側に進めていくうちに視野が悪くなった場合は，1針追加して吊り上げることで良好な視野の確保につながる．

〔男性症例の場合〕（図7）

男性の症例では骨盤底がトンネル状に奥深い症例がよくある．前壁剝離の際はトンネルの天井となる精嚢・前立腺が落ち込んで視野の妨げとなる．これは主に腹膜反転部以下の剝離の際に問題となるが，膀胱直腸窩近傍の腹膜に直針をかけて腹側方向に牽引することで前壁の術野展開をサポートすることができる．

恥骨上の体外から直針付きの2-0ナイロン糸を刺入し，左右1か所ずつ腹膜にかけて腹側に吊り上げることで骨盤底トンネルの天井を持ち上げることができる．腹膜に直針を通す際には，精嚢が透見できるくらいまで先に前壁を剝離しておいて，精嚢実質も貫通させるように直針をかけることでより深い前壁の視野も確保することができる．

考　察

腹腔鏡下大腸癌手術は従来の開腹手術と比較して低侵襲で整容性に優れているとされ，予後に関しても開腹手術に劣らないとする比較試験の結果が報告されている[4~7]．このため，結腸・直腸S状部癌（RS）に対しては腹腔鏡下手術が一般的手技となりつつある．

直腸癌の腹腔鏡下手術と開腹との比較試験の結果はほとんど報告されていないが，腹腔鏡下直腸癌手術の全国アンケートにおける中期成績（Ra，Rb，Pも含む）の結果では生存に関しては開腹手術と差がなく，安全性に関しても合併症の頻度は低いと報告された[8]．現在，直腸癌に対する腹腔鏡下手術が開腹手術に比べて有効性・安全性について劣っていないことを検証する目的で，大腸癌研究会の腹腔鏡下大腸切除研究会で「Clinical Stage 0-Ⅰ期直腸癌に対する腹腔鏡下手術の妥当性に関する第Ⅱ相試験」が行われている[3]．適応に関しては慎重になる必要があるが，この試験の結果も参考にして，今後，腹腔鏡下直腸癌手術は比較的早期の癌から，さらには進行癌にまで適応を拡大して増加していくと考えられる．

当院でも早期から腹腔鏡下直腸癌手術を導入しているが，初期の段階では手術時間が開腹手術と比較して長くなることが多かった．しかし，腹腔鏡下前方切除術における手技の定形化を念頭に置いて手術を施行することでラーニングカーブが短縮され，2008年度には62例の腹腔鏡下前方切除術を施行し，平均手術時間223分，開腹移行率は1.6%という成績であった．また，40例以上の術者経験によって約50分の手術時間短縮が認められた[9]．

このように手技の安定してきた腹腔鏡下前方切除術においても前壁の剝離に関しては困難な場合があり，様々な工夫をして良好な視野を得る必要がある．今回呈示した方法をさらに工夫したり新たなデバイスを用いたりすることによって，直腸前壁のさらに良好な視野を得ることが望まれる．

今後，腹腔鏡下直腸癌手術においては基本手技の習熟とともに，新たな技術の導入によって手術を良好な視野で容易に行うようにしていくことが望まれる．

おわりに

本論文の内容は第 22 回日本内視鏡外科学会総会（2009 年 12 月，東京）において発表した．

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(2010 年 3 月 10 日受付，2010 年 6 月 8 日受理)

Ann Surg Oncol (2010) 17:973–980
DOI 10.1245/s10434-009-0849-y

Annals of
SURGICAL ONCOLOGY
OFFICIAL JOURNAL OF THE SOCIETY OF SURGICAL ONCOLOGY

ORIGINAL ARTICLE – COLORECTAL CANCER

Is Total Mesorectal Excision Always Necessary for T1–T2 Lower Rectal Cancer?

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ABSTRACT

Background. The goal of this multicenter study was to clarify the determinants of local excision for patients with T1–T2 lower rectal cancer.

Methods. Data from 567 consecutive patients who underwent radical resection for T1–T2 lower rectal cancer at 12 institutions between 1991 and 1998 were reviewed. Rates of lymph node metastasis were investigated using a tree analysis, which was hierarchized using independent risk factors for nodal involvement.

Results. The independent risk factors for lymph node metastasis were female gender, depth of tumor invasion, histology other than well-differentiated adenocarcinoma, and lymphatic invasion. According to the first three parameters that can be obtained preoperatively, only 0.99% of the patients without risk factors had lymph node metastasis. On the other hand, even if the lower rectal cancer was at stage T1, women with histological types other than well-differentiated adenocarcinoma had an approximately 30% probability of having lymph node metastasis. Lymphatic invasion was most useful to predict nodal involvement among patients with T2 lower rectal cancer. The rates of lymph node metastasis in T2 patients with and without lymphatic invasion were 32.9% and 9.1%, respectively.

Conclusions. Gender is one of the most important predictors for lymph node metastasis in patients with early distal rectal cancer. Three parameters, including depth of tumor invasion, histology, and gender, are useful determinants for local excision. Additional studies are required to establish the minimum optimal treatment for T2 lower rectal cancer.

Total mesorectal excision (TME) has recently achieved excellent oncological outcomes for patients with rectal cancer.[1] The oncological outcome of rectal cancer is usually worse than that of colon cancer; one reason for this is the higher local recurrence rate after curative resection for rectal cancer.[2] Although TME has decreased the risk of local recurrence, some patients with rectal cancer undergo abdominoperineal resection (APR) followed by permanent colostomy. Some patients develop complications after radical resection for rectal cancer, despite sphincter-sparing procedures.

Local excision is an important treatment option for early distal rectal cancer, because complications can arise after

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First Received: 23 June 2009;
Published Online: 1 December 2009

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radical resection. However, one of the problems associated with local excision for rectal cancer is the unsatisfactory oncological outcome. The reported local recurrence rates after local excision for T1 and T2 tumors range from 6.6% to 18% and from 17% to 37%, respectively.[3–7] A recent study found that patients with T1 rectal cancer treated by local excision have a threefold to fivefold higher risk of tumor recurrence than those treated by radical resection.[3]

Criteria for local excision to treat early rectal cancer have not been established. In this study, the indication of local excision for patients with T1–T2 lower rectal cancer was examined using a model hierarchized with independent risk factors for lymph node metastasis.

PATIENTS AND METHODS

We enrolled 567 patients with T1–T2 lower rectal cancer who underwent curative resection at 12 institutions (all members of the Japanese Society for Cancer of the Colon and Rectum) between 1991 and 1998. The local ethics committee of each institution approved this study. Lower rectal cancer was defined as the distal margin of tumor located below the peritoneal reflection. All patients received tumor-specific mesorectal excision (TSME), meaning that the rectum and mesorectum were removed with an appropriate distal resection margin of >2 cm. Patients who underwent transanal local excision or endoscopic mucosal resection were excluded from this study. Other exclusion criteria were cancers associated with ulcerative colitis, Crohn's disease, or familial adenomatous polyposis.

Preoperative investigations included barium enema examination, colonoscopy, endoscopic ultrasonography, chest x-ray, ultrasonography (US), and/or computed tomography (CT) of the liver, as well as blood tests for carcinoembryonic antigen (CEA). Five- to 10-year postoperative follow-up at most of the participating institutions comprised serum tumor marker measurements every 3 months for the first 3 years and every 6 months for the next 2 years, hepatic imaging (US and/or CT) and chest x-rays every 3 to 6 months, and annual or biennial pelvic CT and colonoscopy.

We analyzed the risk factors for lymph node metastasis in 567 patients who underwent radical resection. To determine the criteria for local excision in patients with T1–T2 lower rectal cancer, the rates of lymph node metastasis were compared according to the number of risk factors for lymph node metastasis.

STATISTICAL ANALYSIS

Data were statistically analyzed using the StatView 5.0 statistical package (Abacus Concepts, Inc., Berkeley, CA). All data are expressed as median ± standard deviation. Associations between each parameter and lymph node metastasis were analyzed using the χ^2 test. Independent risk factors for lymph node metastasis were determined using logistic regression analysis. Differences in numbers of lymph node metastases were analyzed using the Mann–Whitney U test between two groups and by the Kruskal–Wallis test among three or more groups. The actuarial survival of the patients was calculated using the Kaplan–Meier method, and overall survival rates in all groups were compared using the log-rank test. Statistical significance was established at $P < 0.05$ for all results.

RESULTS

Table 1 shows the characteristics of the participating patients. Surgical procedures, tumor size, histology of the primary rectal tumor, rate of lymph node metastasis, and lymphatic and venous invasion significantly differed between patients with T1 and T2 rectal cancer.

Risk Factors for Lymph Node Metastasis

The rates of lymph node metastasis in patients with T1 and T2 lower rectal cancer were 8.6% and 25.7%, respectively. Parameters, such as gender, age, tumor size and histology, T-factor, lymphatic invasion, and venous invasion, were analyzed as potential risk factors for lymph node metastasis in 567 patients with T1–T2 lower rectal cancer scheduled for radical resection. Univariate analysis revealed that female gender ($P = 0.0006$), histology ($P < 0.0001$), T factor ($P < 0.0001$), lymphatic invasion ($P < 0.0001$), and venous invasion ($P < 0.0001$) were risk factors for lymph node metastasis (Table 2). Multivariate analysis revealed that female gender ($P = 0.0009$), histology ($P = 0.017$), T-factor ($P = 0.0085$), and lymphatic invasion ($P < 0.0001$) were independent risk factors for lymph node metastasis in patients with early lower rectal cancers (Table 2).

Tree Analysis of the Rate of Lymph Node Metastasis

The 567 patients with T1–T2 lower rectal cancer were hierarchized for tree analysis according to preoperatively ascertainable T-factor, gender, and histology (in that order) among the independent risk factors for lymph node metastasis (Fig. 1). The rates of lymph node metastasis according to the number of risk factors were 0.99%, 10.6–15.5%, 26.3–30.4%, and 37.3% in patients with zero, one, two, and all three risk factors, respectively. Only 1 of 101 patients without any factors had lymph node metastasis. On the other hand, even if women had T1 lower rectal cancer, 30.4% of those with histological types other than well-differentiated adenocarcinoma had lymph node metastasis.

TABLE 1 Clinicopathologic characteristics of 567 patients with T1–T2 lower rectal cancer

Parameters	T1 (%)	T2 (%)	*P* value
Gender			
Male	144/346 (41.6)	202/346 (58.4)	NS
Female	89/221 (40.3)	132/221 (59.7)	
Age (yr)			
<61	118/288 (41.0)	170/288 (59.0)	NS
≥61	115/278 (41.4)	163/278 (58.6)	
Unknown		1	
Surgical procedure			
APR	28/141 (19.9)	113/141 (80.1)	<0.0001
Hartmann	3/9 (33.3)	6/9 (66.7)	
LAR	202/417 (48.4)	215/417 (51.6)	
Size (cm)			
≤2	128/173 (74.0)	45/173 (26.0)	<0.0001
>2	98/386 (25.4)	288/386 (74.6)	
Unknown	7	1	
Histology			
Well-differentiated Adenocarcinoma	167/327 (51.1)	160/327 (48.9)	<0.0001
Others	64/238 (26.9)	174/238 (73.1)	
Unknown	2		
Lymph node metastasis			
Absent	213/461 (46.2)	248/461 (53.8)	<0.0001
Present	20/106 (18.9)	86/106 (81.1)	
Lymphatic invasion			
Absent	142/241 (58.9)	99/241 (41.1)	<0.0001
Present	86/320 (26.9)	234/320 (73.1)	
Unknown	5	1	
Venous invasion			
Absent	169/317 (53.3)	148/317 (46.7)	<0.0001
Present	59/244 (24.2)	185/244 (75.8)	
Unknown	5	1	

APR abdominoperineal resection, *LAR* low anterior resection, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, or mucinous adenocarcinoma

Multivariate analysis revealed that female gender, histological type other than well-differentiated adenocarcinoma, and venous invasion were independent risk factors for lymph node metastasis in patients with T1 lower rectal cancer (Table 3). Lymphatic invasion and gender were independent risk factors for nodal involvement among patients with T2 lower rectal cancer (Table 4). Figure 2 shows a tree analysis of the lymph node metastasis rate, including lymphatic invasion as a risk factor. The rate of lymph node metastasis in patients without lymphatic invasion was 9.1%.

Number of Lymph Node Metastases

We examined a median of 19 lymph nodes in 87 (15.3%) and 20 (3.5%) patients with N1 and N2 metastases, respectively. The numbers of lymph node metastases in 567 patients with T1–T2 lower rectal cancer and zero, one, two, and three risk factors (Fig. 3) were 0 ± 0.1 (0–1), 0 ± 1.1 (0–11), 0 ± 1.8 (0–13), 0 ± 3.2 (0–26), respectively. The number of lymph node metastases significantly differed among the four groups according to the number of risk factors ($P < 0.0001$) but not between patients with two and three risk factors.

Recurrence in Patients with T1–T2 Lower Rectal Cancer

During a median follow-up period of 4.9 ± 2.3 years, the local recurrence rates among patients with T1 and T2 lower rectal cancer were 2.1% (5/233) and 6.0% (20/334), respectively. Among these 25 patients, 12, 1, 3, 3, and 4 of them underwent curative resection, palliative resection, radiotherapy, and chemoradiotherapy together with chemotherapy, respectively. Two patients did not receive any treatment. The median survival after recurrence was 19

TABLE 2 Risk factors for lymph node metastasis in 567 patients with T1–T2 lower rectal cancer determined by univariate and multivariate analysis

Parameters	No. of lymph node metastasis (%)	Univariate analysis			Multivariate analysis		
		P value	OR	95% CI	*P* value	OR	95% CI
Gender							
Male	49/346 (14.2)	0.0006	1		0.0009	1	
Female	57/221 (25.8)		2.50	1.62–3.85		2.18	1.38–3.46
Age (yr)							
<61	57/288 (19.8)	NS	1				
≥61	49/278 (17.6)		0.867	0.57–1.32			
Unknown	1						
Size (cm)							
≤2	25/173 (14.5)	NS	1				
>2	80/386 (20.7)		1.55	0.95–2.53			
Unknown	8						
Histology							
Well-differentiated adenocarcinoma	39/327 (11.9)	<0.0001	1		0.017	1	
Others	67/238 (28.2)		2.89	1.87–4.48		1.79	1.11–2.88
Unknown	2						
T-factor							
T1	20/233 (8.6)	<0.0001	1		0.0085	1	
T2	86/334 (25.7)		3.69	2.20–6.21		2.13	1.22–3.77
Lymphatic invasion							
Absent	15/241 (6.1)	<0.0001	1		<0.0001	1	
Present	91/320 (28.4)		5.99	3.37–10.65		3.95	2.11–7.46
Unknown	6						
Venous invasion							
Absent	40/317 (12.6)	<0.0001	1		NS	1	
Present	66/244 (27.0)		2.57	1.66–3.97		1.25	0.76–2.07
Unknown	6						

OR odds ratio, *CI* confidence interval, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, or mucinous adenocarcinoma

(range, 3–61) months. Total recurrence rates in this study were 3.4% (8/233) and 12.3% (41/334) among patients with T1 and T2 lower rectal cancer, respectively.

Prognosis of Patients with T1–T2 Lower Rectal Cancer

Relapse-free ($P = 0.0016$) and overall ($P = 0.011$) survival significantly differed between patients with T1 and T2 rectal cancer (Fig. 4). The 5-year relapse-free and overall survival rates were 90.6% and 91.7% in patients with T1 tumors and 82.6% and 86.8% in those with T2 tumors, respectively.

DISCUSSION

The oncological outcome of radical resection for rectal cancer has improved since the adoption of TME.[8] A reasonable quality of life and curability is required to treat patients with rectal cancer, especially those with lower rectal cancer. Therefore, early distal rectal cancer has been treated by local excision in some patients, despite the absence of definitive criteria for local excision. Because the rates of lymph node metastasis in rectal cancer range from 6.5–18% in T1 and 17–38% in T2, respectively, selecting the appropriate surgical procedure for patients with early rectal cancer by predicting lymph node metastasis is important.[6,9–11]

The present study demonstrated that gender, in addition to depth of tumor invasion, histological type, and lymphatic invasion, is a predictive marker for lymph node metastasis in early lower rectal cancer. Approximately 1% of men with well-differentiated T1 adenocarcinoma of the lower rectum had lymph node metastasis. Such patients are suitable candidates for local excision. On the other hand, the rate of lymph node metastasis in women with histological types other than

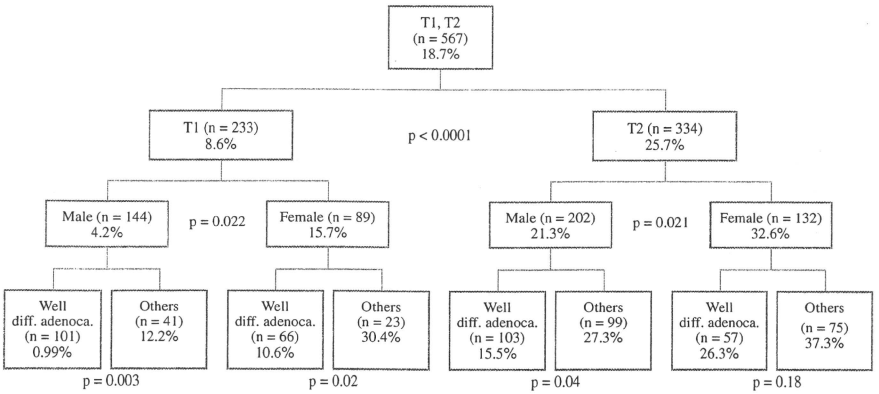

FIG. 1 Rates of lymph node metastasis in patients with T1–T2 lower rectal cancer hierarchized by depth of tumor invasion, gender, and histologic type as risk factors

TABLE 3 Risk factors for lymph node metastasis in 233 patients with T1 lower rectal cancer

Parameters	No. of lymph node metastasis (%)	Univariate analysis *P* value	Multivariate analysis *P* value	OR	95% CI
Gender					
Male	6/144 (4.2)	0.0022	0.0019	1	
Female	14/89 (15.7)			5.68	1.90–16.9
Age (yr)					
<61	13/118 (11.0)	NS			
≥61	7/115 (6.1)				
Size (cm)					
≤2	14/128 (10.9)	NS			
>2	5/98 (5.1)				
Unknown	7				
Histology					
Well-differentiated adenocarcinoma	8/167 (4.8)	0.0007	0.010	1	
Others	12/64 (18.8)			1.5	1.4–11.1
Lymphatic invasion					
Absent	6/142 (4.2)	0.0018	0.059	1	
Present	14/86 (16.3)			2.87	0.96–8.62
Unknown	5				
Venous invasion					
Absent	9/169 (5.3)	0.0018	0.041	1	
Present	11/59 (18.6)			2.99	1.04–8.55
Unknown	5				

OR odds ratio, *CI* confidence interval, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, or mucinous adenocarcinoma

well-differentiated adenocarcinoma was 30.4%, even when the tumor did not invade the muscularis propria. Therefore, radical resection should be indicated for these patients. The reason why female gender is one of the risk factors for nodal involvement in T1–T2 rectal cancer is unclear in the present study. One of the possible

TABLE 4 Risk factors for lymph node metastasis in 334 patients with T2 lower rectal cancer

Parameters	No. of lymph node metastasis (%)	Univariate analysis *P* value	Multivariate analysis *P* value	OR	95% CI
Gender					
Male	43/202 (21.3)	0.021	0.033	1	
Female	43/89 (32.6)			2.18	1.38–3.46
Age (yr)					
<61	44/170 (25.9)	NS			
≥61	42/163 (25.8)				
Unknown	1				
Size (cm)					
≤2	11/45 (24.4)	NS			
>2	75/288 (26.0)				
Unknown	1				
Histology					
Well-differentiated adenocarcinoma	31/160 (19.4)	0.011	0.14	1	
Others	55/174 (31.6)			1.5	0.88–2.56
Lymphatic invasion					
Absent	9/99 (9.1)	<0.0001	0.0001	1	
Present	77/234 (32.9)			4.65	2.11–10.2
Unknown	1				
Venous invasion					
Absent	31/148 (20.9)	0.069	0.92	1	
Present	55/185 (29.7)			0.97	0.55–1.71
Unknown	1				

OR odds ratio, *CI* confidence interval, *Others* moderately differentiated adenocarcinoma, poorly differentiated adenocarcinoma, or mucinous adenocarcinoma

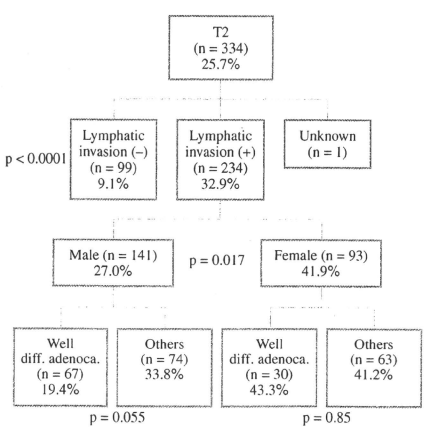

FIG. 2 Classification tree for risk of lymph node metastasis in patients with T2 lower rectal cancer

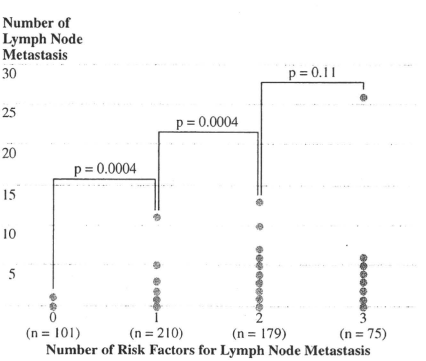

FIG. 3 Number of lymph node metastases according to numbers of risk factors

explanations might be a hormone, such as estrogen. Estrogen receptor is expressed in approximately 70% of colorectal adenocarcinoma.[12] Moreover, a previous study demonstrated that tamoxifen inhibited metastasis from colorectal cancer in a murine model.[13]

Further studies are required to determine therapeutic strategies for patients with T1 lower rectal cancer. Radical resection might be feasible from the viewpoint of

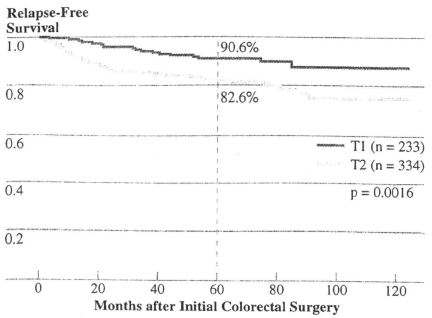

FIG. 4 Relapse-free survival after radical resection for T1 and T2 lower rectal cancer

oncological outcome, although the quality of life worsens after radical surgery compared with that after local excision. Local excision with informed consent would be one option for such patients.

Others have reported local recurrence rates of 4% to 18% after local excision alone for T1 rectal cancer, although those rates were >10% in most studies.[3,4,14–18] Furthermore, local recurrence rates after the local excision with adjuvant therapy in patients with T1 rectal cancer were 0% to 38%.[14,18–21] An optimal indication for local excision in patients with T1 rectal cancer is urgently required. The present study suggests that approximately 40% of patients with T1 lower rectal cancer could have avoided radical resection if the present classification had been applied. Additional studies are necessary to validate our data along with a large-scale, randomized, controlled study to compare the outcomes of radical resection and local excision with adjuvant therapy, such as radiation.

The present study also demonstrated that risk factors for lymph node metastasis, such as gender, histologic type, and the depth of tumor invasion, also are useful to predict numbers of lymph node metastases. Fewer risk factors for lymph node metastasis mean less development of lymph node metastasis. These findings also suggest that gender, histologic type, and depth of tumor invasion are useful to distinguish which patients should be indicated for local excision of early distal rectal cancer.

Lymphatic invasion was the most relevant risk factor to lymph node metastasis in patients with T2 lower rectal cancer. The rates of lymph node metastasis in men and women with T2 lower rectal cancer without lymphatic invasion were 8.3% and 10.3%, respectively. The feasibility of local excision for these patients should be carefully considered, because the present standard therapy for T2 lower rectal cancer seems to be radical resection. However, an initial option for these patients could be local excision. After a pathological examination, careful follow-up under informed consent or chemoradiotherapy might be indicated for patients without lymphatic invasion. On the other hand, radical resection should be added for patients with lymphatic invasion, because the rate of lymph node metastasis for such patients in this study was >30%. Others have reported 5-year local recurrence rates of 15% to 24% in patients with T2 rectal cancer after local excision and adjuvant therapy.[14,18–20,22,23]

The American College of Surgeons Oncology Group is presently conducting a phase II trial of neoadjuvant chemoradiation and local excision for uT2uN0 rectal cancer. The purpose of that study is to determine the rate of disease-free survival at 3 years in patients with ultrasound-staged uT2uN0 rectal cancer treated with chemoradiotherapy followed by local excision.[24] While the results of that study are anticipated, more effective therapeutic strategies are clearly required for patients with T2 lower rectal cancer from the perspective of posttreatment quality of life.

CONCLUSIONS

Gender is an independent determinant of lymph node metastasis in patients with early distal rectal cancer. The combination of gender, histologic type, and depth of tumor invasion is useful to determine indications for local excision in these patients. However, radical resection ought to be recommended for patients with T2 lower rectal cancer. Additional studies should establish the minimum optimal treatment for early distal rectal cancer.

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